Risk profiles for genital infection in women

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Abstract

***Objective*—To determine independent risks with predictive value for specific sexually transmitted diseases in women.**

***Design*—A prospective study of reported sexual behaviour in patients who presented for screening and diagnosis of sexually transmitted diseases.**

***Setting*—A genitourinary medicine clinic at the West London Hospital.**

***Subjects*—1025 consecutive newly attending patients who completed a sexual behaviour questionnaire between February and June 1982.**

***Main outcome measures*—Sexual behaviour reported by standardised self-administered questionnaire and sexually transmitted diseases diagnosed by routine clinical and laboratory methods.**

***Results*—Independent risks for gonorrhoea were teenage (RR 2·0), black race (RR 2·0), more than two partners in the past year (RR 2·2) and previous pregnancy (RR 2·1). Trichomoniasis (RR 2·5), chlamydial infection (RR 1·8) and pelvic inflammatory disease (RR 4·8) also had significant predictive value. Conversely, gonorrhoea proved a risk for chlamydial infection (RR 2·1) together with age under 25 years (RR 2·3) and more than five partners in the previous year (RR 2·2). Ano-genital herpes was predicted by a total of more than 10 sexual partners (RR 2·6) and by both anal (RR 2·2) and oral intercourse (RR 2·9). Age under 25 years was the only independent risk for ano-genital warts (RR 2·0). We found no evidence that either vaginal candidosis or bacterial vaginosis were sexually transmitted. The risk for any genital infection was increased by more than one sexual partner in the preceding year (RR 1·7) and black race (RR 2·0).**

***Conclusions*—Sexually transmitted diseases show both similarities and differences in the risk factors associated with their transmission. These risk profiles facilitate the targeting of health education measures for those sections of the community at greatest risk and form a baseline for the future assessment of the effects of condom protected sexual intercourse and other safer sexual practices.**

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Introduction

Several studies have looked at the relationship between demographic and behavioural variables and specific sexually transmitted infections. Most work has concentrated on HIV infection,[1–5] but studies have also looked at hepatitis B,[6] syphilis,[6] genital herpes,[7–9] gonorrhoea,[10–13] trichomoniasis,[14] chlamydial infection,[12 13 15] bacteriae vaginosis[16] and human papillomavirus (HPV) infection.[17] No study has looked at the full spectrum of sexually transmitted diseases (STD) in a group of women investigated for this purpose. The following study was undertaken in 1982 when condoms were used for contraception by only 4% of women.[18] It therefore presents an unrepeatable opportunity to examine risk profiles for STD, prior to public awareness of HIV infection and before health education on safer sexual behaviour, at a time when condom usage would have had very little influence on transmission of infection. Our findings thus provide a baseline for the risks of unprotected intercourse against which the effects of increasing condom use and other safer sexual practices may be measured.

Patients and methods

Consecutive newly attending women at the Genitourinary Medicine Clinic in West London Hospital were asked to complete a self-administered questionnaire on sexual behaviour.[18] The study began in February 1982 and was continued until the recruitment target of 1,000 fully completed questionnaires had been reached. The data on age, contraception and pregnancy were collected from the clinical records together with the past history and current diagnosis of STD and other genital diseases.

All women were routinely screened by microscopy for vaginal candidosis, trichomoniasis, bacterial vaginosis and gonorrhoea. Ano-genital warts and pelvic inflammatory disease (PID) were diagnosed clinically and cultures were taken for *Candida albicans Trichomonas vaginalis, Neisseria gonorrhoeae, Chlamydia trachomatis* and, when clinically indicated by erosion or ulceration, for herpes simplex virus. The culture media used were Sabouraud's medium for *C. albicans*, Feinberg-Whittington medium for *T. vaginalis*, modified New York City medium for *N. gonorrhoeae* and cell culture for *C. trachomatis*. Serological testing for syphilis was also routine using the Venereal Diseases Research Laboratory Test (VDRL) and the Treponema Pallidum Haemagglutination Test (TPHA).

Data were analysed to assess differences between women found to have specific genital infections and women in whom no genital infection was present. Combinations of genital infections were not analysed.

Statistical analysis employed SPSS-X software and the Charing Cross and Westminister Medical School's Sun 4/670 computer system. The statistical tests used were the chi square test with Yates' correction and Fisher's exact test for univariate analysis and stepwise logistic regression for multivariate analysis. The entry criterion for the model was $p < 0.05$, and the removal criterion $p \geq 0.05$.

Results

The study ran from the 4 February to the 5 June 1982 during which time 1150 consecutive new female patients attended the clinic. Of these women, 65 did not receive the questionnaire because of young age, comprehension of English or individual reluctance or inadvertent omission on the part of medical staff. Of the remaining 1,085 women who received a questionnaire, 42 (4%) failed to complete it fully and 18 (2%) refused to answer either all or in part. There were thus 1025 fully completed questionnaires forming the basis of the study.

The age range was 14–75 years (mean 25·5; median 24). 873 (85%) were white, 131 (13%) were black and 21 (2%) were Asian. There were 784 single women (77%), 134 married (13%) and 101 separated or divorced (10%) and six were widowed (1%). Four hundred and eighteen women had been pregnant (41%) of whom 250 (60%) had had a baby and 168 (40%) had aborted or been terminated. Contraception was not used by 253 women (25%); 525 (51%) used oral contraception, 107 (10%) used an intrauterine contraceptive device (IUCD), 58 (6%) used a cap and 37 (4%) used condoms. Of those not using contraception, 32 (3%) reported that they were sterile or had had a hysterectomy. Accordingly, 25% of the study group had made no attempt to prevent pregnancy.

Table 1 Women with and women without genital infection: demographic and behavioural variables.

Variable	*Women with genital infection (%) n=788*	*Women without genital infection (%) n=237*
Mean Age (years)	25·33	26·28
<20	155 (19·7)	38 (16·0)
<25	448 (56·9)	122 (51·5)
Race White	661 (83·9)	212 (89·5)
Black	111 (14·1)	20 (8·4)
Single	608 (77·2)	176 (74·3)
Contraception:		
Nil	188 (23·9)	65 (27·4)
Pill	418 (53·0)	107 (45·1)
IUCD	78 (9·9)	29 (12·2)
Condom	31 (3·9)	6 (2·5)
Cap	40 (5·1)	8 (17·6)
Past pregnancy	315 (40·0)	103 (43·5)
Menarche: <13	279 (35·4)	90 (38·0)
Coitarche:		
<16	121 (15·4)	38 (16·0)
<17	279 (35·4)	77 (32·5)
Sexual partners:		
Last year		
<1	468 (59·4)	115 (48·5)
>2	250 (31·7)	64 (27·0)
>5	46 (5·8)	11 (4·6)
Lifetime:		
>10	720 (91·4)	209 (88·2)
>5	363 (46·1)	107 (45·1)
>10	174 (22·1)	57 (24·1)
Anal intercourse:		
Penetration	151 (19·2)	49 (20·7)
Ejaculation	66 (8·4)	24 (10·1)
Oral intercourse:		
Penetration	547 (69·4)	167 (70·5)
Ejaculation	291 (36·9)	87 (36·7)

Univariate analysis

The variables used in this analysis are shown in table 1 together with the numbers of women (%) in each category. Women found to have genital infection are listed separately from those who had no genital infection.

The infections examined can be subdivided into three groups: gonorrhoea, chlamydial infection and PID affect the cervix and upper genital tract; trichomoniasis candidosis and bacterial vaginosis affect the vagina; ano-genital herpes and warts may be found anywhere in the lower genital tract. The 237 women with no evidence of genital infection formed the group with which each infection was compared.

Table 2 shows the probability factors (p values) derived from the chi square test or Fisher's exact test for each variable in relation to each specific genital infection. The numbers of women in each infection group are shown at the top of the appropriate column. Negative associations are marked by asterisk and significant values are underlined.

The cervical infections, but not PID, were found especially in women who were under 25 years of age, single, black and commenced intercourse before the age of 17 years (table 2). Gonorrhoea had a negative association with the cap ($p = 0.005$) but not with the condom ($p = 1.0$).

Trichomoniasis showed an association similar to gonorrhoea in respect of black race ($p < 0.0001$), but vaginal candidosis showed no significant association with any of the variables studied. Conversely, bacterial vaginosis showed a negative association with teenage ($p = 0.04$) and early menarche ($p = 0.02$). Anogenital herpes revealed a number of important associations with anal and oral intercourse and larger numbers of lifetime sexual partners. Anogenital warts showed a negative association with the cap ($p = 0.02$) and the pill ($p = 0.003$), but positive associations with age under 25 years ($p = 0.01$) and past pregnancy ($p = 0.03$).

Multivariate analysis

Stepwise logistic regression was performed using seven specific genital infections, a clinical diagnosis of PID and women in whom no infection was detected as dependent variables. A total of 32 variables were entered into each separate model (table 3). In addition to the 24 demographic and behavioural variables used in the univariate analysis, the eight infection variables were added for multivariate analysis in order to examine for possible associations between individual diseases and the risk that one disease might have for another. The logistic regression adjusts the associations for confounding variables, and

Table 2 Comparison between women with specific genital infections or PID and women without any genital infection (n=237): Univariate analysis by chi square test/Fisher's exact test (p values only are given).

	Genital Infections							
Variables	*NG n = 91*	*CT n = 175*	*PID n = 22*	*TV n = 99*	*CA n = 236*	*BV n = 40*	*HSV n=58*	*HPV n=65*
Mean Age (years)	23·9	22·7	23·5	25·4	25·4	26·7	26·3	23·7
Age:								
<20	0·001	0·01	0·2†	0·3	0·5	0·04*	0·6	0·05
<25	0·02	<0·0001	0·6	0·6	0·3	0·2	0·9	0·01
Race:								
White	0·0002*	0·1	0·5†	0·0004*	0·08	0·8†	0·8	0·6
Black	<0·0001	0·02	1·0†	<0·0001	0·1	0·8†	1·0†	1·0
Single	0·04	0·002	1·0	0·6	0·9	1·0	0·5	0·3
Contraception:								
Nil	0·8	0·2	0·5	0·3	0·4	0·9	0·2	1·0
Pill	0·5	0·001	0·9	0·7	0·1	0·9	0·1	0·03*
IUCD	0·7	0·01	0·2†	0·6	0·1	1·0†	0·9	0·9
Condom	1·0	0·4	1·0†	1·0†	0·1	1·0†	0·7†	0·3†
Cap	0·005*†	0·1	0·4†	0·2	0·4	0·5†	1·0†	0·02*†
Past pregnancy	0·1	0·3	0·05	0·3	0·5	1·0	1·0	0·03*
Menarche <13	0·6	0·5	0·5	0·5	0·7	0·02	0·9	0·6
Coitarche:								
<16	0·08	0·2	0·08†	0·1	0·2	0·1	0·4	1·0
<17	0·004	0·002	0·06	0·05	1·0	0·1	0·4	0·8
Sexual partners:								
Last year								
>1	0·07	0·001	0·3	0·1	0·07	0·8	0·002	0·05
>2	0·01	0·05	0·5	0·05	0·5	0·9	0·01	0·8
>5	0·2	0·03	1·0†	0·3	0·5	1·0†	0·05†	0·3†
Lifetime								
>1	0·1	0·08	0·5†	0·6	1·0	0·6†	0·04	0·3
>5	1·0	1·0	0·5	0·9	0·8	0·9	0·01	0·9
>10	0·6	0·7	0·9	1·0	0·7	1·0	0·003	0·4
Anal intercourse:								
Penetration	0·1	1·0	1·0	0·6	0·7	1·0	0·01	0·8
Ejaculation	0·2	1·0	0·7†	0·7	0·4	0·6†	0·05	0·5
Oral intercourse:								
Penetration	0·05	1·0	0·7	0·4	0·7	0·3	0·004	0·9
Ejaculation	0·01*	0·7	1·0	0·6	0·9	1·0	0·03	0·4

NG = gonorrhoea; CT = chlamydial infection; PID = pelvic inflammatory disease; TV = trichomoniasis; CA = vaginal candidosis; BV = bacterial vaginosis; HSV = anogenital herpes; HPV = anogenital warts.
*Negative association. †Fisher's exact Test.

Table 3 Relative risks for various genital infections: Stepwise logistic regression with genital infections as dependent variables.

Variables	*Probability (p) value*	*Relative risk (RR)*	*95% Confidence intervals*	
			Lower	*Upper*
Gonorrhoea				
Black race	0·02	2·0	1·1	3·6
Age <20 years	0·01	2·0	1·2	3·4
Partners >2 in last year	0·002	2·2	1·3	3·6
Oral ejaculation	0·01	0·5	0·3	0·9
Past pregnancy	0·005	2·1*	1·3	3·4
Chlamydial infection	0·03	1·8	1·1	3·0
Trichomoniasis	0·002	2·5	1·4	4·4
PID	0·002	4·8	1·7	13·1
Chlamydial infection				
Age <25 years	<0·0001	2·3	1·5	3·4
Partners >5 in last year	0·01	2·2	1·2	4·0
IUCD	0·04	0·4	0·2	0·9
Gonorrhoea	0·004	2·1	1·3	3·4
PID				
Past pregnancy	0·01	3·4*	1·4	8·6
Gonorrhoea	<0·0001	7·3	2·9	18·3
Trichomoniasis				
Black race	0·0001	2·8	1·7	4·8
No contraception	0·03	1·7*	1·1	2·8
IUCD	0·01	2·3*	1·2	4·4
Gonorrhoea	0·001	2·6	1·5	4·6
Vaginal candidosis				
Coitarche <16 years	0·04	0·6*	0·4	0·99
Condom	0·01	2·4*	1·2	4·8
Bacterial vaginosis	0·01	0·08	0·01	0·6
Bacterial vaginosis				
Age <20 years	0·04	0·1	0·02	0·9
Menarche <13 years	0·02	0·4	0·2	0·9
Vaginal candidosis	0·01	0·08	0·01	0·6
Angenital herpes				
Coitarche <17 years	0·03	0·5*	0·3	0·9
Total partners >10	0·001	2·6	1·5	4·7
Anal ejaculation	0·03	2·2*	1·1	4·5
Fellatio	0·02	2·9	1·2	7·0
Anogenital warts				
Age <25 years	0·01	2·0	1·1	3·5
Any infection				
Black race	0·01	2·0	1·3	3·3
Partners >1 in last year	0·002	1·7	1·3	2·0

*Not significant on univariate analysis.

may either reveal risk factors obscured by confounding or eliminate risk factors produced by confounding. Table 3 shows the statistically significant risk factors for each disease.

Cervical infections and PID

Teenagers (RR, 2·0), black race (RR, 2·0), a history of past pregnancy (RR, 2·1) and of more than two partners in the previous year (RR 2·2) had an increased risk of gonorrhoea. The practice of fellatio with oral ejaculation significantly decreased risk of gonorrhoea (RR 0·5). The independent associations with chlamydial infection (RR 1·8), PID (RR 4·8) and trichomoniasis (RR 2·5) re-enforce clinical experience.

Women under 25 years of age (RR 2·3) and women who had more than five partners in the preceding year (RR 2·2) were at greater risk of chlamydial infection. Co-existent gonorrhoea has been reported previously and was confirmed as a risk (RR 2·1), but IUCD usage showed a protective effect (RR 0·4).

Past pregnancy (RR 3·4) was revealed as an increased risk for PID only after stepwise logistic regression analysis and this might have been concealed on univariate analysis by the age related occurrence of pregnancy. However, the high risk from gonococcal infection (RR 7·3) emphasised the morbidity of this condition.

Vaginal infections

Women of black race proved to be at increased risk of trichomoniasis as they were

of gonorrhoea. The relative risks related to non-use of contraception (RR 1·7) and the use of the IUCD (RR 2·3) have no immediately obvious explanation, the latter relationship appearing only on multivariate analysis. Oral contraception may, like the cap and the condom, protect against this infection. On the other hand, the clinical association between trichomoniasis and gonorrhoea is well known (RR 2·6). Trichomonal infection does not persist in most men and must therefore be transmitted to another partner within a few days in order to survive. Likewise, the transmission of gonorrhoea demands similar behaviour because of the short incubation period for symptomatic urethritis in the male.

Coitarche under 16 years (RR 0·6) appeared to protect against vaginal candidosis, but condom use increased the risk (RR 2·4). Teenagers (RR 0·1) and women whose menarche was before the age of 13 (RR 0·4) were less at risk of developing bacterial vaginosis, which together with an inverse relationship with vaginal candidosis (RR 0·08) seems likely to relate to the pathophysiology of the condition. None of these variables relates directly to sexual transmission.

General genital infections

A total of more than 10 partners (RR 2·6), anal intercourse with ejaculation (RR 2·2) and fellatio without ejaculation (RR 2·9) each constituted an independent risk for anogenital herpes. Only 22·5% of women in the study reported more than 10 partners in their lifetime which makes it likely that this risk relates to the chance of finding a partner with active herpetic infection.

Ano-genital warts showed no independent risk factors related to sexual behaviour or other genital infections but occurred more frequently in women under 25 (RR 2·0. This is consistent with a highly prevalent infection acquired in the early years of sexual activity to which immunity subsequently develops. The largest single group of women in the study were found not to be suffering from any genital infection. More than one sexual partner (RR 1·7) and black race (RR 2·0) were both independent risk factors for the presence of genital infection.

Discussion

This study emphasises the multifactorial nature of risks for STD, together with their inherent diversity. Previous studies on demography, reproductive behaviour and sexual behaviour have concentrated on one or two diseases rather than the whole range of common diseases and only about half of the non-HIV studies reviewed employed multivariate analysis to eliminate confounding variables.[7 8 13 14 17] Most studies have taken place in the United States of America where ethnicity, low income and social deprivation may have a greater impact on reproductive and sexual behaviour than in the United Kingdom.[7–11 14 17] Moreover, the variety of settings has meant that they have examined different subgroups of the population at risk. In the United Kingdom, almost all women suffering from real or suspected STD attend departments of genitourinary medicine, which provide a free and confidential service offering open access and rapid diagnosis and treatment. Women attending such clinics will have the highest incidence of STD and provide the best means for defining those at highest risk and in greatest need of targeting for health education.

We have confirmed the increased risk run by teenagers and black women for gonorrhoea.[10] This was further enhanced by previous pregnancy and the presence of chlamydial infection, trichomoniasis and symptomatic PID. Risks for chlamydial infection were fewer and consisted of age less than 25 years, more than five partners in the previous year and gonorrhoea. Each infection therefore appeared to potentiate the other. The protective effects are more difficult to interpret. Oral ejaculation (RR 0·5) may protect against gonorrhoea by diverting potential infection from the genital tract to the pharynx where it may spontaneously resolve. An IUCD (RR 0·4) may enhance local immunity as a foreign body or may accelerate squamous metaplasia of columnar epithelium and so reduce the epithelial surface susceptible to chlamydial infection. The risk observed for PID from previous pregnancy (RR 3·4) is likely to relate to dilatation of the external os and consequent impairment of the cervical barrier to ascending infection. Early coitarche was eliminated as a risk factor for gonorrhoea and chlamydial infection by logistic regression.

In contrast to cervical infection, vaginal infections showed no risk factors in common with each other. Indeed, our findings confirmed the inverse relationship between vaginal candidosis and bacterial vaginosis reported by Moi.[16] This accords with the pathophysiology of these conditions which confines the diagnosis of bacterial vaginosis to a vaginal pH >4·5, while most candidal infections occur below this pH. Resistance to candidal infection may well be promoted by earlier coitarche (RR 0·6) as a consequence of earlier menarche in recent generations of young women.[18] This more physiologically natural sequence of events may in turn enhance the immune competence of the cervix and also have been responsible for the protection against bacterial vaginosis seen in teenagers (RR 0·1) and women with early menarche (RR 0·4). Conversely, the significantly increased risk associated with condom use (RR 2·4), while not previously reported, is entirely consistent with reaction to the physico-chemical effects of a vaginal foreign body lowering resistance to a ubiquitous pathogen. Enhanced risk for trichomoniasis found in black women[12] may, like gonorrhoea, lie in the behaviour of male partners rather than the women themselves, who reported fewer partners than white women.[18]

Our findings with regard to anogenital herpes are unique in that this infection is the only one to carry a substantial risk from

multiple lifetime partners. It is also the only chronic relapsing STD which may be intermittently infectious over a long period of time so that multiple partners longterm could be expected to increase the likelihood of its acquisition. The mechanisms of risk from anal intercourse with ejaculation and from fellatio are not difficult to explain. Minor trauma is known to predispose to herpes simplex infection and local injury to the epithelium is likely to be caused by anal intercourse. An increasing proportion of genital isolates have been of the oral type (HSV-I) and since oral intercourse (both fellatio and cunnilingus) has been reported to be practised by a majority of sexually active young people,[19] orogenital transfer is predictable. Prior fellatio may also render penile lesions more infectious, although transmission is more likely to result from mutual orogenital contact. The protective effect of early coitarche could operate through risk reduction afforded by cross-immunity from previous HSV-I infection declining with time.

We have reported previously the association between cervical wart virus infection and age under 25 years.[20] A recent study using the polymerase chain reaction showed a 46% prevalence of genital human papilloma virus (HPV) infection in young women at university, but only 10% had past or current genital warts and in only two thirds of these was HPV detected.[17] The independent associations with HPV infection included age under 26 years, black race, oral contraception and increased numbers of sexual partners. It would appear, therefore, that the only risk shared with clinical ano-genital warts is young age.

It was salutary to find that any more than a single sexual partner in the preceding year carried a risk for the acquisition of STD, but more disturbing that women of black race were equally at risk. Barrier contraception was used by less than 10% of women in our study, but provided no evidence of risk reduction for the common STD. Future studies will show the effect of increasing condom use on risk profiles for STD in women.

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